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| 09/424,482      | 02/29/2000  | YEN CHOO             | PM264974            | 8038             |

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EXAMINER

WESSENDORF, TERESA D

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1639

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/424,482

Applicant(s)

CHOO ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,6,7 and 27-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 6-7 and 27-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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**DETAILED ACTION**

***Status of Claims***

Claims 1-2, 6-7 and 27-34 are pending and under examination.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35

U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 6-7 and 27-34, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. [This is a new matter rejection.]

Claim 1 drawn to the randomization of amino acids at position 2 restricted to amino acids selected from the group consisting of D,A,R,Q,H,K,S,N is not supported in the as-filed specification. Likewise, claim 30 wherein the randomization of amino acid at position 6 is restricted to the recited amino acid

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residues is not supported in the as-filed specification. The as-filed specification does not recite that the specific amino acids at either position two or six can be grouped with any amino acids at the other recited positions e.g., -1, 1, 3, 4, 5 and so forth. Rather, the specification recites that the specifically recited amino acids at either positions two or six is grouped with the specific amino acid residues at the different positions of the polypeptide as recited in e.g., claim 7. MPEP 714.02 states that applicants specifically point where in the specification the new claimed limitations appear.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 32 are unclear as to the limitation of selecting the randomized positions from positions -1, 1, 2, 3, and 6. If -1, for example, is selected how does it extend to

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cover position 6? These claims are confusing as applied to the amended base claims 1 and 30.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 103***

Claims 1-2, 6-7 and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greisman et al (Science, Ref 97) in view of and Choo et al (Current Opinion in Biotechnology) for reasons advanced in the last Office action.

***Response to Arguments***

Applicants maintain the distinctions over the cited references described in their appeal brief and will resubmit them on appeal if necessary. However, it is submitted that such should be unnecessary in view of the amendment of the claim specifying sets of amino acids to which partial randomization is restricted.

In response, the arguments presented in the last Office action addressing the Appeal brief will similarly be relied upon on resubmission of the appeal brief. Applicants' further arguments are not commensurate in scope with the claims. The claims do not recite for a set of amino acid to which partial randomization is restricted.

As previously noted by applicants the present application provides the insight that varying positions 6 and 2 together is advantageous in generating additional specificities not obtained by varying a single finger alone because these residues contact the same base pair of a target (specification at p. 9, lines 5-9). However, only certain residues occupying positions 6 and 2 are able to act in combination to result in zinc finger proteins with sequence specific binding. Restriction of partial randomization to such amino acids is advantageous, both because it increases the representation of productive combinations of amino acids at these positions, and because it allows greater variation at other positions without exceeding constraints on overall library size.

In reply, except for claim 7, none of the claims recite certain residues that occupy positions 6 and 2 simultaneously to provide the argued above advantages and sequence specific binding.

Applicants argue that Greisman teaches to randomize in such a manner as to allow any of sixteen amino acids at each position (footnote 15 of Greisman). The four omitted amino acids are omitted as part of a strategy to avoid stop codons (id.). Applicants argue that Choo does not explicitly disclose whether he restricted randomization to certain codons. However,

reference to his earlier work cited in the Choo paper (see reference 7 fourth paragraph of the Choo paper) shows that he, like Greisman, restricted randomization to sixteen amino acids. A patent by Choo, US 6,007,988 (of record) also omitted four amino acids and explained that the reason was to avoid stop codons ("T in the first base position is omitted in order to avoid stop codons, but this has the unfortunate effect that the codons for Trp, Phe, Tyr and Cys are not represented" (at col. 12, 24-27, emphasis supplied). The view that omitting the above amino acids was "unfortunate" teaches away from performing randomization with additional amino acids omitted. None of the references teaches the claimed groups of amino acids to which randomization should be restricted.

In response, there is nothing in the claims to preclude the 16 amino acid randomization taught by Greisman or Choo. The claims recite "comprising amino acid positions from -1 to 9" with randomization that extends to cover positions 6 and 2. Applicants' use of the word "comprising" does not preclude the presence of other amino acid residues present in the prior art. It has been long held that the use of the term "comprising" leaves a claim open for inclusion of materials other than those recited in the claims". Ex parte Davis, 80 USPQ 448.

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Simply because some codon has been omitted such that the amino acids W, F, Y, C has not been represented is not a teaching away from the randomization of the other residues, as claimed. Choo discloses at page 432, col. 2 a library of a middle finger in which the seven positions (-1, 1, 2, 3, 5, 6 and 8) were randomized. Choo further discloses at page 433 last paragraph that the best combination of fingers was selected *en bloc* using the entire 9bp target site. Thus, the disclosure of Choo of *en bloc* combinations in the specific positions -1 to +6 would lead one having ordinary skill in the art to the claimed combination. Thus, at the time of applicants' invention *en bloc* combination of amino acids is known in the art. As Choo states this *en bloc* combination partly circumvent the problems of position and context. As held by the majority in *Merck & Co. Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 10 USPQ 2d 1843 (Fed. Cir. 1989), at 10 USPQ 2d 1846:

That the '813 patent discloses a multitude of effective combinations does not render any particular formulation less obvious. This is especially true because the claimed composition is used for the identical purpose taught by the prior art. See *In re Corkill*, 771 F.2d 1496, 1500, 226 USPQ 1005, 1008 (Fed. Cir. 1985) (obviousness rejection of claims affirmed in light of prior art teaching that "hydrated zeolites will work" in detergent formulations, even though "the inventors selected the zeolites of the claims from among "thousands of compounds"); *In re Susi*, 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971).



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In the absence of new and unexpected results in picking and choosing to combine positions 6 and 2, the claimed invention is prima facie obvious to one having ordinary skill in the art at the time the invention was made. Synergism is simply too broad to provide a useful yardstick with which to measure patentability. ....the overall performance of the combination is always equal to the sum of the functions of the individual components. *Chore-time Equipment, Inc. V. Cumberland Corp.* 218 USPQ 673 (Fed. Cir. 1983).

No claim is allowed.

#### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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T.D. Wessendorf  
Primary Examiner  
Art Unit 1639

Tdw

July 12, 2005